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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,420	12/19/2001	Mike Levanduski	326.1001	2519

7590 01/24/2005

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EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 01/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/026,420	LEVANDUSKI, MIKE	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-76* is/are pending in the application.

4a) Of the above claim(s) *1-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *57-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/05/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 11/30/04 has been acknowledged.

Claims 1-76 are pending.

Claims 1-56 are withdrawn.

Claims 57-76 are examined in this office action.

*Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is **571-273-8300**.*

Election/Restrictions

Applicant's election without traverse of Group VII (claims 56-76) in the reply filed on 11/30/04 is acknowledged.

Claims 1-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/30/04.656

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 69-71 and 73-74 rejected under 35 U.S.C. 102(b) as being anticipted by Stice et al (US 5945577, 1999).

The invention of instant claims is drawn to method of producing an enucleated oocyte wherein the polar body and nuclear DNA had been removed by breaching zona pelucida of the oocytes.

Stice teaches a method of nuclear transfer that involves the transplantation of a donor differentiated cell nuclei into enucleated oocyte of same species. The cited art teaches the nuclear transfer units for making multiple genotypes and transgenic offspring and for the production of isogenic embryonic and non-embryonic stem cells (abstract). Regarding claim 69 the cited art teaches harvesting oocytes from females and maturing the oocytes to metaphase II before enucleating the oocytes (col. 9, line 44-65). Regarding claim 73 the cited art teaches the cited art further teaches that enucleation is accomplished microsurgically using a micropipette to remove the polar body and the adjacent cytoplasm. The oocytes are then screened to identify those of which have been successfully enucleated (col. 9 lines 30-55). Removal of polar body and nuclear DNA as disclosed herein inherently encompasses the breaching of zona pellucida. Regarding claims 70-71 the cited art teaches that scope enucleated oocytes encompasses oocytes from a mammalian source that includes sheep, cows, pigs, horses, rabbits, guinea pigs, mice, hamsters, rats and primates including human (col.8 lines 10-43, colo.4 lines 30-33). Regarding claim 74 the cited art teaches the removal of oocytes cytoplasm during enucleation procedure, which lead to an oocytes that are smaller than the size of original oocytes. Thus given the broadest reasonable interpretation the cited art clearly anticipate the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 72 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stice (EP0559307 A1, 1993) as applied to claim 69, 71 and 73-74 above, and further in view of Ji et al (Theriogenology 54:827-834, 2000).

Stice teaches a method of nuclear transfer that involves the transplantation of a donor differentiated cell nuclei into enucleated oocyte of same species. The cited art further teaches the nuclear transfer units for making multiple genotypes and transgenic offspring and for the production of isogenic embryonic and non-embryonic stem cells (abstract). Regarding claim 69 the cited art teaches harvesting oocytes from females and maturing the oocytes to metaphase II before enucleating the oocytes (col. 9, line 44-65). Regarding claim 73 the cited art teaches the cited art further teaches that enucleation is accomplished microsurgically using a micropipette to remove the polar body and the adjacent cytoplasm. The oocytes are then screened to identify those of which have been successfully enucleated (col. 9 lines 30-55). Removal of polar body and nuclear DNA as disclosed herein inherently encompasses the breaching of zona pellucida. Regarding claims 70-71 the cited art teaches that scope enucleated oocytes encompasses oocytes from a mammalian source that includes sheep, cows, pigs, horses, rabbits, guinea pigs, mice, hamsters, rats and primates including human (col.8 lines 10-43, colo.4 lines 30-33). Regarding claim 74-76 the cited art teaches the removal of oocytes cytoplasm during enucleation procedure, which lead to an oocytes that are smaller than the size of original oocytes.

Even though Stice teaches a method of making enucleated oocytes, the cited art does not teach the removal or breaching of zona pellucida from oocytes using a chemical agent.

Ji teaches that zona pellucida is an outer membrane that encloses the mammalian ovum, which plays an important role in the initial stages of fertilization but is

not required for embryonic development. The cited art teaches the removal of zona pellucida, using 0.05% pronase, 0.05% trypsin or acid Tyrode's solution (page 828 para.4, page 831, fig-1 and 2). The cited art further teaches that removal of zona pellucida has practical applications such as providing a means for virus mediated gene transfer into the ovum or early stage embryo lacking zona pellucida (page 828, para.1).

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the method of Stice by substituting the enucleated oocytes with enucleated zona pellucida free oocytes. One would have been motivated to do so introduce virus mediated gene transfer into the ovum or during early stage embryo development. One would have a reasonable expectation of success because removal of zona pellucida using a chemical agent has been routine in the art at the time the instant invention was made. In addition removing zona pellucida facilitates the virus mediated gene transfer and has no detrimental effects on embryonic development. Thus the invention as claimed is *prima facie* obvious in view of cited prior art of record.

Claims 75-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stice et al (US 5945577, 1999) in view of Ji et al (Theriogenology 54:827-834, 2000 as applied to claims 69-74 above, and further in view of Massey US 5057420, 1991 and Parther et al (US 4994384, 1991).

As stated above combined teaching of Stice et al and Ji et al suggests the subject matter of invention as claimed in claims 69-74. However the Stice and Ji do not teach splitting of enucleated oocytes (with or without zona pellucida) into smaller oocytes (ooplastoids).

Massey teaches a method of slitting enucleated oocytes wherein ½, ¼ or 1/8 of ooplasm has been removed using a micropipette (col.3 lines 32-53, col. 6-8). Similarly Prather et al teaches enucleation of oocytes by aspirating ½ of the cytoplasm juxtaposed to the polar body using a 25-35 micron transfer pipette (col. 6, line 22-38).

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the teaching of Stice and Ji by aspirating different amount of ooplasm, which would yield enucleated oocytes having about 15% to about 50% volume of the

original oocytes. One would have been motivated to do so in order to make fragments of enucleated oocytes. One would have been also motivated to do so in order to remove host oocytes genetic material. One would have a reasonable expectation of success because sling oocytes and removal of ooplasm has been routine in the art at time the instant invention was made. Thus the invention as claimed is *prima facie* obvious in view of cited prior art of record.

Claims 57-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stice et al (US 5,945,577, 1999) in view of Ji et al (Theriogenology 54:827-834, 2000).

The instant claims are drawn to a method of producing pluripotent non-embryonic stem cells comprising nuclear transfer of somatic cell nuclei into an enucleated oocyte.

Stice teaches a method of nuclear transfer that involves the transplantation of a donor differentiated cell nuclei into enucleated oocyte of same species. The cited art further teaches the nuclear transfer units for making multiple genotypes and transgenic offspring and for the production of isogenic embryonic and non-embryonic stem cells (abstract). The cited art further teaches that embryonic stem cells are capable of differentiating in non-embryonic stem cells like hematopoietic stem cells (col. 13 lines 30-67, col. 14, lines 1-67). Regarding claims 57-58 specifically the cited art teaches obtaining source donor nuclei and enucleated oocytes from same species (col.7 lines 9-33, col. 9-10, col.16 lines 61-). Regarding claim 59-60 the cited art further teaches that the somatic cell or somatic nucleous is obtained from mature mammalian cells comprising epithelial cell, lymphopcytes and fibroblasts (col.8 lines 4-43). Regarding claims 61-62 and 68 the cited art teaches isolation of single enucleated oocytes followed by nuclear transfer of donor nucleus via intra cytoplasmic injection (col9. line 40-55). Regarding claim 63-68 the cited art teaches fusion of enucleated oocytes with a mammalian cell using an electrofussion technique (col. 9, line 56-67, col.10, lines 1-52).

Even though Stice teaches a method of producing pluripotent non-embryonic stem cells comprising nuclear transfer of somatic cell nuclei into enucleated oocytes, the cited art fails to teach the removal of zona pellucida from oocytes.

Ji teaches that zona pellucida is an outer membrane that encloses the mammalian ovum, which plays an important role in the initial stages of fertilization but is not required for embryonic development. The cited art teaches the removal of zona pellucida, using 0.05% pronase, 0.05% trypsin or acid Tyrode's solution (page 828 para.4, page 831, fig-1 and 2). The cited art further teaches that removal of zona pellucida has practical applications such as providing a means for virus mediated gene transfer into the ovum or early stage embryo lacking zona pellucida (page 828, para.1).

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the method of Stice by substituting the enucleated oocytes with enucleated zona pellucida free oocytes. One would have been motivated to do so introduce virus mediated gene transfer into the ovum or during early stage embryo development. One would have a reasonable expectation of success because removal of zona pellucida using a chemical agent has been routine in the art at the time the instant invention was made. In addition removing zona pellucida facilitates the virus mediated gene transfer and has no detrimental effects on embryonic development. Thus the invention as claimed is *prima facie* obvious in view of cited prior art of record.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance.

Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547.** For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300.**

Sumesh Kaushal
Examiner GAU 1636

SUMESH KAUSHAL
PATENT EXAMINER